REMARKS

In view of the above amendments and the following remarks, the Examiner is respectfully requested to allow claims 77-85, the currently pending claims. Claims 1-76 are canceled without prejudice to refilling of the original scope. Claim 77 is amended. Applicants respectfully request reconsideration of the rejections.

The specification has been amended to delete the term "figure 613".

In view of the cancellation of claims 1-76, rejections of the claims are made moot and will not be further considered.

Claims 77-83 have been rejected under 35 U.S.C. 112, second paragraph. The Office Action states that the body of the claims recite an additive, not a synergistic, combination. Without conceding to the correctness of the rejection, in order to further prosecution Applicants have clarified the meaning of the term "synergistic" by addition of the claim language "a level more than additive when compared to administration of the adenovirus vector and antineoplastic agent alone". Support for the amending language may be found in the specification at page 21, lines 25-29.

Claims 77-83 have been rejected under 35 U.S.C. 103 as reading on an additive combination, and as such are rejected as obvious over Henderson *et al.* taken with Gurnani *et al.* or over Henderson *et al.* taken with Gurnani *et al.* in further view of Duque *et al.*

Applicants respectfully submit that, in view of the above amendments and following remarks, the present claims are directed to a synergistic combination of adenovirus vector and antineoplastic agent. The synergy found by Applicants was unexpected, and could not have been predicted by one of skill in the art prior to the disclosure of the present application.

Table 5 of the subject application reports that the following antineoplastic agents were synergistic with the adenovirus defined by the present claims, wherein an adenoviral gene essential for replication is under transcriptional control of a prostate-specific antigen (PSA)-TRE, and wherein said target tumor cell-specific adenovirus results in virus replication-dependent cytolysis.

Table 5: Synergistic Effects of CV787/Chemotherapeutic Combinations

VIRUS	TARGET/ CELL LINE	CHEMOTHERAPEUTIC AGENT	CLASS OF AGENT	SYNERGY
CV787	Prostate cancer/ LNCaP	5-Fluorouracil (5-FU)	Antimetabolites (acting as pseudosubstrate for essential enzymatic reactions)	Yes
CV787	Prostate cancer/ LNCaP	Cisplatin	Alkylating agent (Platinum-containing agents - Causing single- and double-strand break in DNA)	Yes
CV787	Prostate cancer/ LNCaP	Doxorubicin	Antibiotics (anticycline; interrupting DNA replication and transcription, causing strand break)	Yes
CV787	Prostate cancer/ LNCaP	Estramustine	Alkylating agent	Yes
CV787	LNCaP	Etoposide	Plant alkaloid (inhibiting the assembly of microtubules and disrupting mitosis	Yes
CV787	Prostate cancer/ LNCaP	Mitoxantrone	Antibiotics (anticycline)	Yes
CV787	Prostate cancer/ LNCaP	TAXOTERE™ (docetaxel)	Plant alkaloids	Yes
CV787	Prostate cancer/ LNCaP	TAXOL™ (paclitaxel)	Plant alkaloids	Yes

The evidence provided in the Figures supports Table 5. For example, a synergistic effect for the compounds shown in Table 5 is supported by the Figures as follows: a combination of 5-FU and adenovirus CV787 (Figure 9); a combination of Cisplatin and adenovirus CV787 (Figure 8);a combination of Doxorubicin and adenovirus CV787 (Figure 7); a combination of Estramustine and adenovirus CV787 (Figure 27); a combination of Etoposide and adenovirus CV787 (Figure 6); a combination of Mitoxantrone and adenovirus CV787 (Figure 5); a combination of docetaxel) and adenovirus CV787 (Figures 3 and 4); and a combination of paclitaxel and adenovirus CV787 (Figure 2) A review of the level of tumor suppression in these figures makes it apparent that the suppression with the combined therapy is greater than the additive effects of the individual agents.

Even if, *arguendo*, one of skill in the art would have expected a beneficial effect from the combined agents, it could not have been predicted based on the teachings of Henderson *et al.* in view of Gurnani *et al.* that the combined effect would be greater than additive.

The teachings of Duque *et al.* do not remedy the deficiencies of Henderson *et al.* and Gurnani *et al.* Although Duque *et al.* teach the deletion of the 19 kDa region, there is no indication that combinations of alkaloids and adenovirus specific for prostate cells would provide for a greater than additive suppression of tumor growth.

In view of the above amendments and remarks, withdrawal of the rejection is requested.

CONCLUSION

Applicants submit that all of the claims are now in condition for allowance, which action is requested. If the Examiner finds that a Telephone Conference would expedite the prosecution of this application, she is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any other fees under 37 C.F.R. §§ 1.16 and 1.17 which may be required by this paper, or to credit any overpayment, to Deposit Account No. 50-0815, order number CELL-017.

Respectfully submitted,

Date: 02-23-2004

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